

Amendments to the Specification

Please replace the paragraph beginning at page 1, line 9 with the following two paragraphs:

This application is a continuation-in-part of U.S. Appl. No. 09/189,702, filed November 10, 1998, which is herein incorporated by reference; and is a continuation-in-part of U.S. Appl. No. 08/347,610, filed December 1, 1994, which is herein incorporated by reference; and is a continuation-in-part of U.S. Appl. No. 08/205,713, filed March 4, 1994, which is herein incorporated by reference; said Appl. No. 08/347,610 is a continuation-in-part of Appl. No. 08/159,339, filed November 29, 1993, U.S. Patent No. 6,037,135, which is herein incorporated by reference, which is a continuation-in-part of Appl. No. 08/103,396, filed August 6, 1993, abandoned, which is herein incorporated by reference; said Appl. No. 08/205,713 is a continuation-in-part of Appl. No. 08/159,184, filed November 29, 1993, abandoned, which is herein incorporated by reference, which is a continuation-in-part of Appl. No. 08/073,205, filed June 4, 1993, abandoned, which is herein incorporated by reference, which is a continuation-in-part of Appl. No. 08/027,146, filed March 5, 1993, abandoned, which is herein incorporated by reference.

~~This application is a Continuation-In-Part ("CIP") of U.S.S.N. 09/189,702 filed 11/10/98, which is a CIP of U.S.S.N. 08/205,713 filed 3/4/94, which is a CIP of 08/159,184 filed 11/29/93 and now abandoned, which is a CIP of 08/073,205 filed 6/4/93 and now abandoned, which is a CIP of 08/027,146 filed 3/5/93 and now abandoned.~~

The present application is also related to U.S.S.N. 09/226,775, which is a CIP of U.S.S.N. 08/815,396, which claims the benefit of U.S.S.N. 60/013,113, now abandoned. Furthermore, the present application is related to U.S.S.N. 09/017,735, which is a CIP of

abandoned U.S.S.N. 08/589,108; abandoned U.S.S.N. 08/753,622, abandoned U.S.S.N. 08/822,382, abandoned U.S.S.N. 60/013,980, U.S.S.N. 08/454,033, U.S.S.N. 09/116,424, and U.S.S.N. 08/349,177. The present application is also related to U.S.S.N. 09/017,524, U.S.S.N. 08/821,739, abandoned U.S.S.N. 60/013,833, abandoned U.S.S.N. 08/758,409, abandoned U.S.S.N. 08/589,107, U.S.S.N. 08/451,913, U.S.S.N. 08/186,266, issued as U.S. Patent No. 5,662,907, and abandoned U.S.S.N. 09/116,061, ~~and U.S.S.N. 08/347,610, which is a CIP of U.S.S.N. 08/159,339, which is a CIP of abandoned U.S.S.N. 08/103,396, which is a CIP of abandoned U.S.S.N. 08/027,746, which is a CIP of abandoned U.S.S.N. 07/926,666.~~ The present application is also related to U.S.S.N. 09/017,743, abandoned U.S.S.N. 08/753,615; abandoned U.S.S.N. 08/590,298, abandoned U.S.S.N. 09/115,400, and U.S.S.N. 08/452,843, which is a CIP of U.S.S.N. 08/344,824, which is a CIP of abandoned U.S.S.N. 08/278,634. The present application is also related to abandoned provisional U.S.S.N. 60/087,192 and U.S.S.N. 09/009,953, issued as U.S. Patent No. 6,413,517, which is a CIP of abandoned U.S.S.N. 60/036,713 and abandoned U.S.S.N. 60/037,432. In addition, the present application is related to abandoned U.S.S.N. 09/098,584, U.S.S.N. 09/239,043, and to abandoned Provisional U.S. Patent Application 60/117,486 filed 1/27/99. The present application is also related to ~~U.S. Patent Application entitled "Inducing Cellular Immune Responses to Hepatitis C Virus Using Peptide and Nucleic Acid Compositions", Attorney Docket No. 018623-0013910~~ U.S.S.N. 09/350,401, filed 7/8/99. All of the above applications in this paragraph are herein incorporated by reference.

Please replace the paragraph beginning at page 19, line 13 with the following paragraph:

An affinity threshold associated with immunogenicity in the context of HLA class II DR molecules has also been delineated (*see, e. g.,* Southwood *et al. J Immunology* 160: 3363-3373, 1998, and U.S.S.N. 60/087192 filed 5/29/98, now abandoned, but claimed as a priority document to PCT Publication No. WO 99/61916). In order to define a biologically significant threshold of DR binding affinity, a database of the binding affinities of 32 DR-restricted epitopes for their restricting element (i. e., the HLA molecule that binds the motif) was compiled. In approximately half of the cases (15 of 32 epitopes), DR restriction was associated with high binding affinities, i. e. binding affinity values of 100 nM or less. In the other half of the cases (16 of 32), DR restriction was associated with intermediate affinity (binding affinity values in the 100-1000 nM range). In only one of 32 cases was DR restriction associated with an IC_{50} of 1000 nM or greater. Thus, 1000 nM can be defined as an affinity threshold associated with immunogenicity in the context of DR molecules.

Please replace the paragraph beginning at page 52, line 17 with the following paragraph:

For instance, the ability of the peptides to induce CTL activity can be enhanced by linking the peptide to a sequence which contains at least one epitope that is capable of inducing a T helper cell response. The use of T helper epitopes in conjunction with CTL epitopes to enhance immunogenicity is illustrated, for example, in co-pending U. S. S. N. 08/820,360, now abandoned, U. S. S. N. 08/197,484, now issued as U.S. Patent No. 6,419,931, and U. S. S. N. 08/464,234, now abandoned.

Please replace the paragraph beginning at page 82, line 23 with the following paragraph:

The degree to which the plasmid construct prepared using the methodology outlined in Example 11 is able to induce immunogenicity is evaluated through *in vivo* injections into mice and subsequent *in vitro* assessment of CTL and HTL activity, which are analysed using cytotoxicity and proliferation assays, respectively, as detailed *e. g.*, in U. S. S. N. 09/311,784 filed 5/13/99, now issued as U.S. Patent No. 6,534,482, and Alexander *et al.*, *Immunity* 1 : 751-761,1994. For example, to assess the capacity of a pMin minigene construct to induce CTLs *in vivo*, HLA-A11/K^b transgenic mice, for example, are immunized intramuscularly with 100 µg of naked cDNA. As a means of comparing the level of CTLs induced by cDNA immunization, a control group of animals is also immunized with an actual peptide composition that comprises multiple epitopes synthesized as a single polypeptide as they would be encoded by the minigene.